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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
TONGUE, LAKIA J	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 03/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/646,948	ZSEBO ET AL.	
	Examiner	Art Unit	
	Lakia J. Tongue	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-36* is/are pending in the application.

4a) Of the above claim(s) *1-9 and 28-36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10, 11, 13-20, 23-27* is/are rejected.

7)☒ Claim(s) *12,21 and 22* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

HL

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-9, drawn to an immunogenic composition comprising a pharmaceutically acceptable excipient and an attenuated bacteria, classified in class 424, subclass 258.1.

II. Claims 10-27, drawn to an immunogenic composition, classified in class 424, subclass 234.1.

III. Claims 28-31, drawn to a bacteria, classified in class 530, subclass 825.

IV. Claims 32-36, drawn to a method of eliciting an immune response in an individual, classified in class 424, subclass 9.2.

Inventions I and II are related as products. In the instant case inventions I and II are different from each other because invention I has a pharmaceutically acceptable excipient and an attenuated bacteria. However, invention II comprises an inhibitor of a human defensin, a pharmaceutically acceptable excipient and attenuated bacteria. The inventions of invention I and II are different because invention I does not require an inhibitor of a human defensin which is required by invention II.

Inventions I and III are related as products. In the instant case inventions I and III are different from each other because invention I has a pharmaceutically acceptable excipient and an attenuated bacteria, while Invention III has a bacteria with no carrier.

Inventions I and IV are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case invention I (bacteria) can be used in a diagnostic assay.

Inventions II and III are related as products. In the instant case invention II products comprise an inhibitor of a human defensin, a pharmaceutically acceptable excipient and attenuated bacteria. However, invention III comprises genetically modified bacteria.

Inventions II and IV are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case invention II and Iv are different because invention II has a pharmaceutically acceptable excipient and an attenuated bacteria as well as an inhibitor. Invention IV is a method of eliciting an immune response in an individual.

Inventions III and IV are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different

process of using that product (MPEP § 806.05(h)). In the instant case the product can be used in a method of diagnosis.

DETAILED ACTION

In response to the election restriction requirement dated December 10, 2004 without traverse Applicant elected Group II, claims 10-27 for continued examination. Claims 1-9 and 28-36 are withdrawn.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 3/22/04 has been considered by the examiner.

Claim Objections

Claims 10 and 17 are objected to because of the following informalities: Applicant is intending for the limitation of claim 10 to recite an immunogenic composition comprising: a pharmaceutically acceptable excipient and an attenuated bacteria and at least one inhibitor of a human defensin. Applicant has used the punctuation mark (;) which indicates *or* instead of the punctuation mark (,) which indicates *and*. In addition, claim 17 recites the immunogenic composition of claim 10, wherein the bacteria is attenuated by alteration in its Dam gene. At first appearance the acronym Dam should be accompanied by its meaning DNA adenine methylase (DAM). Every

occurrence thereafter can be written using the assigned acronym. Appropriate correction is required.

Claims 12, 21 and 22 are objected to because they depend from rejected-based claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 13 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification broadly describes as part of the invention alpha 1-antichymotrypsin and derivatives thereof and alpha 2-macroglobulin and derivatives thereof. Mutant or variant thereof does not meet the written description provision of 35 USC 112, first paragraph. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" The

specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed."

The skilled artisan cannot envision the detailed chemical structure alpha 1-antichymotrypsin and alpha 2-macroglobulin and therefore conception cannot be achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 10, 13, 15 and 16 are rejected under 35 U.S.C. 102(a) as being anticipated by Arigoni, F. et al (European Patent Application, 1 227 153 A1).

Claims 10, 13, 15 and 16 are drawn to an immunogenic composition comprising: a pharmaceutically acceptable excipient, an attenuated bacteria and at least one inhibitor of a human defensin.

Arigoni et al discloses examples of serpins (inhibitor of human defensin) (page 2, section 0013, 0014). Arigoni et al disclose that recombinant serpins are introduced for expression into suitable host cells such as *E. coli* and *Streptococci* (page 3, section 0023). Lastly, Aragon et al disclose in example 2 a situation where the nucleic acid encoding the putative Bifidobacterial serpin deleted from its signal peptide was cloned into the *E. coli* expression vector and the corresponding protein was produced (page 5, section 0038-39).

Claims 10, 11 and 13-15 rejected under 35 U.S.C. 102(b) as being anticipated by Cooperman et al (U.S. Patent 5,723,316).

Claims 10, 11 and 13-15 are drawn to an immunogenic composition comprising: a pharmaceutically acceptable excipient, an attenuated bacteria and at least one inhibitor of a human defensin.

Cooperman et al discloses several immunogenic compositions comprising a pharmaceutically acceptable excipient, an attenuated bacteria and at least one inhibitor of a human defensin (column 7, lines 56-60, column 12, lines 46-51 and column 12, lines 64-68). One in particular discloses that *E. coli* was transformed in a typical preparation of α-1-antichymotrypsin analogue and dispersed in a potassium phosphate buffer (column 12, lines 64-68). Cooperman et al discloses nucleic acids coding for

recombinant α-1-antichymotrypsin may be expressed in prokaryotic or eukaryotic host cells, including the most commonly used bacterial host cell for the production of recombinant proteins, *E. coli.* Other microbial strains may also be used, such as *Bacillus subtilis,* and other enterobacteriaceae such as *Salmonella typhimurium* or *Serratia marcescens* (column 6, lines 5-11).

Claims 10, 19, 20, 24 and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Auerswald et al (U.S. Patent 4,894,436).

Claims 10, 19, 20 and 24 are drawn to an immunogenic composition comprising: a pharmaceutically acceptable excipient, an attenuated bacteria and at least one inhibitor of a human defensin.

Auerswald et al discloses a buffer for the measurement of trypsin and trypsin inhibitors (column 13, lines 25-27). The particular organism of choice was *E. coli* RR1ΔM15 (column 13, lines 10, 25, 56 and 62-63). Other pharmaceutically acceptable excipients are located in column 14, lines 19-45.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

Claims 14, 15, 17, 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cooperman et al (U.S. Patent 5,723,316) as applied to claims 10, 11, 13 and 15 above, and further in view of Mahan, M. et al (WO 00/45840).

Claims 14, 15, 17, 18 are drawn to an immunogenic composition comprising: a pharmaceutically acceptable excipient, an attenuated bacteria and at least one inhibitor of a human defensin.

Cooperman et al discloses the limitations of claims 11, 13 and 15 above. Cooperman et al does not teach an immunogenic composition wherein the bacteria is attenuated by alteration in its Dam gene and the immunogenic composition wherein the expression of the Dam gene is increased or decrease relative to wild type.

Mahan et al teaches an immunogenic composition comprising live attenuated pathogenic bacteria, such as *Salmonella,* and a pharmaceutically acceptable excipient. The pathogenic bacteria contains a mutation which alters DNA adenine methylase (Dam) activity such that the pathogenic bacteria is attenuated (page 30, lines 17-21). Mahan et al teaches that a pTP166 plasmid that produces *E. coli* Dam at 100-fold wild-type level could be used (page 31, lines 12-13). Mahan et al teaches a wide variety of Salmonella, including *S. typhimurium; S. enteritidis, S. typhi; S. abortus-ovi; S. abortus-equi; S. Dublin; S. gallinarum* or *S pullorum.* Other organisms for which the invention may include *Yersinia spp., Vibrio spp.,* particularly *V. cholerae* and *Shigella spp.*

Cooperman et al and Mahan et al disclose analogous inventions related to an immunogenic composition comprising a pharmaceutically acceptable excipient, an attenuated bacteria and at least one inhibitor of a human defensin. It would have been obvious to one of ordinary skill in the art at the time of invention to modify the invention of Cooperman et al with the teachings of Mahan et al because methylation of DNA

adenine residues is essential for bacterial virulence, thus genes that encode DNA adenine methylases and their products are promising targets for antimicrobial drug development (Mahan, page 15, lines 20-24). In addition it helps to obtain more detailed information regarding bacterium pathogenesis, specifically Salmonella (Mahan, page 15, line 15-18). It would have been expected, barring evidence to the contrary, that the composition would help to elicit a sustained and highly specific immune response.

Claims 23, 26 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Auerswald et al (U.S. Patent 4,894,436) as applied to claim 10, 19, 20 and 24 above, and further in view of Mahan, M. et al (WO 00/45840).

Claims 23, 26 and 27 are drawn to an immunogenic composition comprising: a pharmaceutically acceptable excipient, an attenuated bacteria and at least one inhibitor of a human defensin.

Auerswald et al discloses the limitations of claims 10, 19, 20 and 24 above. Auerswald et al does not teach an immunogenic composition wherein the bacteria is attenuated by alteration in its Dam gene, an immunogenic composition wherein the attenuated bacteria is Salmonella *enterica* selected from the group consisting of serovars *Typhimurium, Enteritidis, Typhi, Abortus-ovi, Abortus-equi, Dublin, Gallinarum* and *Pullorum,* and wherein expression of the Dam gene is increased or decrease relative to wild type.

Mahan et al teaches an immunogenic composition comprising live attenuated pathogenic bacteria, such as *Salmonella,* and a pharmaceutically acceptable excipient. The pathogenic bacteria contains a mutation which alters DNA adenine methylase (Dam) activity such that the pathogenic bacteria is attenuated (page 30, lines 17-21). Mahan et al teaches that a pTP166 plasmid that produces *E. coli* Dam at 100-fold wild-type level could be used (page 31, lines 12-13). Mahan et al teaches a wide variety of Salmonella, including *S. typhimurium; S. enteritidis, S. typhi; S. abortus-ovi; S. abortus-equi; S. Dublin; S. gallinarum* or *S pullorum.* Other organisms for which the invention may include *Yersinia spp., Vibrio spp.,* particularly *V. cholerae* and *Shigella spp.*

Auerswald et al and Mahan et al disclose analogous inventions related to an immunogenic composition comprising a pharmaceutically acceptable excipient, an attenuated bacteria and at least one inhibitor of a human defensin. It would have been obvious to one of ordinary skill in the art at the time of invention to modify the invention of Cooperman et al with the teachings of Mahan et al because methylation of DNA adenine residues is essential for bacterial virulence, thus genes that encode DNA adenine methylases and their products are promising targets for antimicrobial drug development (Mahan, page 15, lines 20-24). In addition it helps to obtain more detailed information regarding bacterium pathogenesis, specifically Salmonella (Mahan, page 15, line 15-18). It would have been expected, barring evidence to the contrary, that the composition would help to elicit a sustained and highly specific immune response.

Status of Claims

Claims 12, 21 and 22 appear to be free of the cited prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lakia J. Tongue whose telephone number is 571-272-2921. The examiner can normally be reached on Monday-Friday 7-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

LJT

L. J. Smith

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